

CLAIM AMENDMENTS:

Claims 1-40, 42, and 43 have been amended, new claim 45 has been added, and claims 41 and 44 have been cancelled. The following listing of claims will replace all prior versions and listings, of claims in this Application:

Listing of Claims:

Claim 1 (Currently amended): A formulated liposome for incorporating a high content of hydrophobic substances therein, comprising:

a first phospholipid[.,] which is selected from a hydrogenated naturally-occurring phospholipid or a saturated phospholipid having with long carbon chains $-(CH_2)_n-$, in which the value of n is at least 14) and which has a phase transition temperature T_{g1} ranging between 40 and 74°C;

a second phospholipid[.,] which is selected from an unsaturated phospholipid or a saturated phospholipid having with short carbon chains $-(CH_2)_n-$, in which the value of n is at most 14) , and which has a phase transition temperature T_{g2} ranging between -30 and 10°C;

liposome-forming materials effective to form a liposome in which the first phospholipid and the second phospholipid coexist in two immiscible phases and create several discontinuous regions, and in which a molar ratio of the first phospholipid to the second phospholipid is at least 3:16; and

one or more hydrophobic substances incorporated in the liposome in an amount of at least 20 mole% to form the formulated liposome.[; and]]

liposome forming materials,

wherein the first phospholipid and the second phospholipid coexist in the liposome in two immiscible phases and create several discontinuous regions, and a molar ratio of the first phospholipid to the second phospholipid is no less than 3/16; a phase transition temperature T_{g1} of the first phospholipid is in the range between 40

and 74°C , and a phase transition temperature T_{g2} of the second phospholipid is in the range between -30 and 10°C wherein while a drug delivery temperature T_1 and a drug storage temperature T_2 are chosen at specified ranges subject to an order of $T_{g1} > T_1 > T_2 > T_{g2}$, and wherein the formulated liposome has an incorporation efficiency which remains at at least about 70% of incorporation efficiency for six months or more.

Claim 2 (Currently amended): The formulated liposome according to claim 1, wherein the phase transition temperature of the first phospholipid is preferably in the range ranges between 50 and 65°C , and the phase transition temperature of the second phospholipid is preferably in the range ranges between -20 and 4°C .

Claim 3 (Currently amended): The formulated liposome according to claim 1, wherein the first phospholipid is selected from the group consisting of phosphatidyl choline (PC), phosphatidyl glycerol (PG), phosphatidyl serine (PS), phosphatidyl acid (PA) and phosphatidyl ethanolamine (PE).

Claim 4 (Currently amended): The formulated liposome according to claim 3, wherein the first phospholipid is selected from the group consisting of hydrogenated egg phosphatidyl choline (HEPC), hydrogenated soy phosphatidyl choline (HSPC), dipalmitoyl phosphatidyl choline (DPPC) and distearoyl phosphatidyl choline (DSPC), diarachidoyl phosphatidyl choline, dimyristoyl phosphatidyl ethanolamine (DMPE), dipalmitoyl phosphatidyl ethanolamine (DPPE), distearoyl phosphatidyl ethanolamine (DSPE), dipalmitoyl phosphatidyl glycerol (DPPG), distearoyl phosphatidyl glycerol, dimyristoyl phosphatidyl acid (DMPA), dipalmitoyl phosphatidyl acid (DPPA), dipalmitoyl phosphatidyl serine (DPPS), and distearoyl phosphatidyl serine (DSPS).

Claim 5 (Currently amended): The formulated liposome according to claim 1, wherein the second phospholipid is selected from the group consisting of phosphatidyl choline

(PC), phosphatidyl glycerol (PG), phosphatidyl serine (PS), phosphatidyl acid (PA) and phosphatidyl ethanolamine (PE).

Claim 6 (Currently amended): The formulated liposome according to claim 5, wherein the second phospholipid is selected from the group consisting of egg phosphatidyl choline (EPC), soy phosphatidyl choline (SPC), oleoyl palmitoyl phosphatidyl choline, dioleoyl phosphatidyl choline, dipetroselinoyl phosphatidyl choline, dipalmitelaidoyl phosphatidyl choline, dioleoyl phosphatidyl ethanolamine, dioleoyl phosphatidyl serine, dilauroyl phosphatidyl choline (DLPC), diundecanoyl phosphatidyl choline, didecanoyl phosphatidyl ethanolamine, and dinonanoyl phosphatidyl ethanolamine.

Claim 7 (Currently amended): The formulated liposome according to claim 1, wherein the hydrophobic substances are one or more hydrophobic pharmaceutical compounds.

Claim 8 (Currently amended): The formulated liposome according to claim 7, wherein the one or more hydrophobic pharmaceutical compound is paclitaxel ~~and/or docetaxel~~.

Claim 9 (Currently amended): The formulated liposome according to claim 8, wherein the paclitaxel and/or docetaxel are/ is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 25 mole%.

Claim 10 (Currently amended): The formulated liposome according to claim 9, wherein the paclitaxel and/or docetaxel are/ is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 11 (Currently amended): The formulated liposome according to claim 9, wherein the paclitaxel and/or docetaxel are/ is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 12 (Currently amended): The formulated liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is retinoic acid and/or a derivative thereof, the retinoic acid derivative is selected from the group consisting of retinol, retinyl acylate and retinyl acetate.

Claim 13 (Currently amended): The formulated liposome according to claim 12, wherein the retinoic acid and/or the derivative thereof are/ is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 40 mole%.

Claim 14 (Currently amended): The formulated liposome according to claim 13, wherein the retinoic acid and/or the derivative thereof are/ is incorporated with a drug/lipid ratio ranging from about 10 mole% to 40 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 15 (Currently amended): The formulated liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is camptothecin and/or a derivative thereof, wherein the derivative of camptothecin is selected from the group consisting of irinotecan, topotecan, SN 38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxycamptothecin.

~~20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy 20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.~~

Claim 16 (Currently amended): The formulated liposome according to claim 15, wherein the camptothecin and/or the derivative thereof are/ is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 30 mole%.

Claim 17 (Currently amended): The formulated liposome according to claim 16, wherein the camptothecin and/or the derivative thereof are/ is incorporated with a drug/lipid ratio ranging from about 5 mole% to 30 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 18 (Currently amended): The formulated liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is selected from the group consisting of paclitaxel and/or a paclitaxel derivative, retinoic acid and/or a retinoic acid derivative, and camptothecin and/or a camptothecin derivative, wherein the derivative of paclitaxel is docetaxel; the retinoic acid derivative is selected from the group consisting of retinol, retinyl acylate and retinyl acetate; the camptothecin derivative is selected from the group consisting of irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxy camptothecin, 9-amino-10,11-methylenedioxy camptothecin, 9-chloro-10,11-methylenedioxy camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy 20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy 20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

Claim 19 (Currently amended): The formulated liposome according to claim 1, wherein the liposome-forming materials are selected from the group consisting of hydrophilic polymer-modified lipids, cholesterol, cholesterol derivatives, antioxidant, and mixtures thereof, wherein cholesterol derivatives are selected from the group consisting of polyethylene glycol 600 mono(cholesteryl) ether sebacate and cholesteryl oleyl carbonate.

Claim 20 (Currently amended): The formulated liposome according to claim 19, wherein the hydrophilic polymer-modified lipid is methoxy polyethylene glycol-distearoyl phosphatidyl ethanolamine (MPEG-DSPE).

Claim 21 (Currently amended): A formulated liposome for incorporating a high content of hydrophobic substances therein, comprising:

a first phospholipid which is optionally a phosphatidyl choline, which is selected from a hydrogenated naturally-occurring phospholipid or a saturated phospholipid having with long carbon chains $-(CH_2)_n-$, in which the value of n is at least 14, and which has a phase transition temperature T_{g1} ranging between 40 and 74°C ;

a second phospholipid which is optionally a phosphatidyl choline, which is selected from an unsaturated phospholipid or a saturated phospholipid having with short carbon chains $-(CH_2)_n-$, in which the value of n is at most 14, and which has a phase transition temperature T_{g2} ranging between -30 and 10°C;

liposome-forming materials effective to form a liposome in which the first phospholipid and the second phospholipid coexist in two immiscible phases and create several discontinuous regions; and

one or more hydrophobic substances incorporated in the liposome in an amount of at least 20 mole% to form the formulated liposome.]; and]]

liposome-forming materials,

~~wherein the first and the second phosphatidyl cholines coexist in the liposome in two immiscible phases and create several discontinuous regions, and a molar ratio of the first phosphatidyl choline to the second phosphatidyl choline is no less than 3/16; a phase transition temperature T_{g1} of the first phosphatidyl choline is in the range between 40 and 74°C, and a phase transition temperature T_{g2} of the second phosphatidyl choline is in the range between -30 and 10°C wherein while a drug delivery temperature T_1 and a drug storage temperature T_2 are chosen at specified ranges subject to an order of $T_{g1} > T_1 > T_2 > T_{g2}$, and wherein the formulated liposome has an incorporation efficiency which remains at at least about 70% of incorporation efficiency for six months or more.~~

Claim 22 (Currently amended): The formulated liposome according to claim 21, wherein the phase transition temperature of the first phospholipid is preferably in the range ranges from 50 to 65°C, and the phase transition temperature of the second phospholipid is preferably in the range ranges from -20 to 4°C.

Claim 23 (Currently amended): The formulated liposome according to claim 21, wherein the first phospholipid is a phosphatidyl choline (PC) and is selected from the group consisting of hydrogenated egg phosphatidyl choline (HEPC), hydrogenated soy phosphatidyl choline (HSPC), dipalmitoyl phosphatidyl choline (DPPC) and distearoyl phosphatidyl choline (DSPC),

Claim 24 (Currently amended): The liposome according to claim 21, wherein the second phospholipid is a phosphatidyl choline (PC) and is selected from the group consisting of egg phosphatidyl choline (EPC), soy phosphatidyl choline (SPC), synthetic or natural-occurring unsaturated phosphatidyl cholines and dilauroyl phosphatidyl

choline (DLPC), oleoyl palmitoyl phosphatidyl choline, dioleoyl phosphatidyl choline, and dipetroselinoyl phosphatidyl choline, dipalmitaidoyl phosphatidyl choline.

Claim 25 (Currently amended): The formulated liposome according to claim 21, wherein the hydrophobic substances are one or more hydrophobic pharmaceutical compounds.

Claim 26 (Currently amended): The formulated liposome according to claim 25, wherein the one or more hydrophobic pharmaceutical compound is at least one of paclitaxel and/or docetaxel a paclitaxel derivative.

Claim 27 (Currently amended): The formulated liposome according to claim 26, wherein the at least one of paclitaxel and/or docetaxel a paclitaxel derivative are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 25 mole%.

Claim 28 (Currently amended): The formulated liposome according to claim 27, wherein the at least one of paclitaxel and/or docetaxel a paclitaxel derivative are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 29 (Currently amended): The formulated liposome according to claim 27, wherein the at least one of paclitaxel and/or docetaxel a paclitaxel derivative are/ is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 30 (Currently amended): The formulated liposome according to claim 25, wherein the one or more hydrophobic pharmaceutical compound is at least one of retinoic acid

and/or a retinoic acid derivative thereof, the retinoic acid derivative is selected from the group consisting of retinol, retinyl acylate and retinyl acetate.

Claim 31 (Currently amended): The formulated liposome according to claim 30, wherein the at least one of retinoic acid and/or the a retinoic acid derivative thereof are/ is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 40 mole%.

Claim 32 (Currently amended): The formulated liposome according to claim 31, wherein the at least one of retinoic acid and/or the a retinoic acid derivative thereof are/ is incorporated with a drug/lipid ratio ranging from about 10 mole% to 40 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 33 (Currently amended): The formulated liposome according to claim 25, wherein the one or more hydrophobic pharmaceutical compound is at least one of camptothecin and/or a camptothecin derivative, and the derivative of camptothecin is selected from the group consisting of irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamine)ethyl)-(20S)-camptothecin.

Claim 34 (Currently amended): The formulated liposome according to claim 33, wherein the at least one of camptothecin and/or the a camptothecin derivative thereof are/ is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 30 mole%.

Claim 35 (Currently amended): The formulated liposome according to claim 34, wherein the at least one of camptothecin and/or the a camptothecin derivative thereof are/ is incorporated with a drug/lipid ratio ranging from about 5 mole% to 30 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 36 (Currently amended): The formulated liposome according to claim 25, wherein the one or more hydrophobic pharmaceutical compound is selected from the group consisting of at least one of paclitaxel and a paclitaxel derivative, at least one of retinoic acid and a retinoic acid derivative, and at least one of camptothecin and a camptothecin derivative the derivatives thereof, wherein the derivative of paclitaxel is docetaxel; the derivatives of retinoic acid are selected from the group consisting of retinol, retinyl acetate and retinyl acetate; the derivatives of camptothecin are selected from the group consisting of irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

Claim 37 (Currently amended): The formulated liposome according to claim 21, wherein the liposome-forming materials are selected from the group consisting of hydrophilic polymer-modified lipids, cholesterol, cholesterol derivatives, antioxidant, and mixture thereof, wherein cholesterol derivatives are selected from the group consisting of polyethylene glycol 600 mono(cholesteryl) ether sebacate and cholesteryl oleyl carbonate.

Claim 38 (Currently amended): The formulated liposome according to claim 37, wherein the hydrophilic polymer-modified lipid is methoxy polyethylene glycol-distearoyl phosphatidyl ethanolamine (MPEG-DSPE).

Claim 39 (Currently amended): The formulated liposome according to claim 1, wherein the one or more hydrophobic substances substance incorporated in the liposome is present in an amount of ranging from about 3 mole% to about 25 mole%.

Claim 40 (Currently amended): The formulated liposome according to claim 1, wherein the one or more hydrophobic substances substance incorporated in the liposome is present in an amount ranging from about 8 mole% to about 25 mole%, ~~and the liposome remains at at least 70% of incorporation efficiency for at least 60 days.~~

Claim 41 (Cancelled).

Claim 42 (Currently amended): The formulated liposome according to claim 21, wherein the one or more hydrophobic substances substance incorporated in the liposome is present in an amount ranging from about 3 mole% to about 25 mole%.

Claim 43 (Currently amended): The formulated liposome according to claim 21, wherein the one or more hydrophobic substances substance incorporated in the liposome is present in an amount ranging from about 8 mole% to about 25 mole%, ~~and the liposome remains at at least 70% of incorporation efficiency for at least 60 days.~~

Claim 44 (Cancelled).

Claim 45 (New): The formulated liposome according to claim 1, wherein the first and second phospholipids are phosphatidyl cholines.

Claim 46 (New): The formulated liposome according to claim 21, wherein the first phospholipid and the second phospholipid are present in a molar ratio of the first phospholipid to the second phospholipid is at least 3:16.